

REMARKS

Favorable consideration and allowance are respectfully requested for claims 1-16 in view of the following remarks. Claims 17 and 18 are withdrawn, without prejudice or any disclaimer of the subject matter therein.

The pending Restriction Requirement is traversed because claims 1-16 should be considered together. The restriction is allegedly justified on grounds that the process of claims 14-18 could be practiced with a product other than the composition of claims 1-13. While claims 17 and 18 do not require the enzyme mixture of claim 1, claims 14-16 certainly do require this same enzyme mixture.

As previously pointed out, MPEP § 806.05(h) states that restriction may be required if a process of use **as claimed** can be practiced with another materially different product. In this case, method claim 14 is dependent from composition claim 1 and by its terms expressly requires administration of the composition according to claim 1. Thus, the process **as claimed** requires use of the claimed composition. The recent Office Action reiterates that other substances can be used for the same general purpose, but this does not establish that the process **as claimed** can be practiced with a materially different product. The process "as claimed" is more specific than just inhibition of maldigestion. The process "as claimed" requires the use of the composition of claim 1. The attempted restriction thus fails to satisfy the explicit requirements of MPEP § 806.05(h). Consequently, the requirement for restriction is improper and cannot stand.

Further, the Office Action of September 13, 2004 acknowledges that "process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right" in accordance with the rejoinder provisions of MPEP § 821.04. Thus, if the Examiner allows the claims of Group I, then claims 14-16 could be rejoined. Claims 14-16 should be allowed

to proceed with the claims of Group I so as to avoid unnecessary withdrawal and rejoinder.

Accordingly, reconsideration and withdrawal of the restriction requirement is respectfully requested with respect to claims 14-16.

The rejection of claims 1-13 under 35 U.S.C. § 103 as obvious over Sipos (U.S. 5,750,104) in view of Ogawa et al. (U.S. 6,013,680) is respectfully traversed.

Claim 1 requires:

- a) a concentrated lipase of *Rhizopus deleamar*,
- b) a neutral protease of *Aspergillus melleus*, and
- c) an amylase of *Aspergillus oryzae*.

The cited references do not satisfy a finding of prima facie obviousness for at least the following reasons: First, there is no teaching or suggestion to one of ordinary skill in the art to combine Sipos and Ogawa et al.. Second, the cited art does not teach or suggest all the claim limitations. The Manual of Patent Examining Procedure (MPEP) requires each of these in § 706.02(j). Patent and Trademark Office, U.S. Department of Commerce, Manual of Patent Examining Procedures, § 706.02(j) (8th ed., Rev. 2, May 2004).

Starting with the Sipos reference, the Office Action asserts that Sipos would teach pharmaceutical compositions for treating digestive disorders comprising lipase of *Rhizopus deleamar* and amylase of *Aspergillus oryzae*. This is simply not the case. Instead, Sipos merely discloses that glycerol ester hydrolase (a lipase) may be used. This is a general type of enzyme which is classified as being "3.1.1.3" according to the Enzyme classification system (EC) as proposed by the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (NC-IUBMB). However, numerous enzymes from various different sources in fact share this common classification "EC

3.1.1.3". Not all of these are a lipase of *Rhizopus deleamar*. At best, the reference teaches a broad genus that might include the claimed species. It cannot be concluded that all those different enzymes might be suitable constituents of an enzyme mixture according to the present invention.

Furthermore, it is expressly stated in the Sipos reference (cf. col 6, lines 22 - 26) that the disclosed enzymes are in fact typically derived from animal sources. In contrast, the enzymes of the present invention are derived from microorganisms. Thus, Sipos actually teaches away from the claimed combination where an enzyme is derived from a microorganism. It is important to note in this context, that enzymes from microorganism sources are an essential feature of the present invention, because it is normally very difficult to achieve very high specific enzymatic activities per dose with digestive enzymes from animal sources.

Similar to the situation with the lipase is the situation with the amylase from *Aspergillus oryzae*, Sipos only teaches that amylases classified as "EC 3.2.1.1." are suitable for the disclosed composition. Again, numerous enzymes from various different sources share this feature and, again Sipos in fact teaches that the enzymes used are typically derived from animal sources, not from microorganisms. Sipos does not teach the amylase of *Aspergillus oryzae* as claimed.

Furthermore, the Sipos compositions require the obligatory presence of 15 to about 60 % w/w of a buffering agent (see Sipos, col 7, lines 7 - 8). The presence of buffering agents reduced the concentration of therapeutically active enzymes and results in a lowered amount of therapeutically active digestive enzymes being available per dosage form. In contrast, an object of the present invention is to provide mixtures of digestive enzymes with a high enzymatic activity which permit the use of relatively low dosage quantities (e.g., p. 5, paragraph [0015] of the specification). This object is not compatible with a Sipos-type composition,

containing high quantities of buffer substances without enzymatic activity. Accordingly, one of skill in the art would not be inclined to look to Sipos for teachings relevant to achieving high enzymatic activity with low dosages.

Referring to the Ogawa et al. reference, this teaches a medicament comprising a histamine H₂ receptor antagonist and/or a proton pump inhibitor, and a digestive enzyme. This composition is therefore different from the composition of the present invention. Further, the use of the Ogawa et al. composition is also different. While Ogawa et al. teach treatments of gastric or duodenal ulcers, the compositions of the present invention are useful to treat digestive enzyme insufficiency or maldigestion, in particular caused by pancreatic insufficiency. Still further, Prozyme 6® is only cited as one example of a wide variety of enzymes of different enzymatic activities which may be suitable for use in a Ogawa et al.-type of composition.

Nothing in this reference would therefore seem to teach or suggest that Prozyme 6® may be selected to improve a digestive enzyme composition for the treatment of (human) digestive enzyme insufficiency, and certainly a person skilled in the art would not have any motivation to combine the teachings of Ogawa et al. and of Sipos so as to arrive at the present invention.

Finally, in the field of enzyme compositions, it is never a routine task to simply interchange one enzyme (e.g. a protease) of a balanced mixture of enzymes with an arbitrarily selected other enzyme thought to have similar activity. The new enzyme must fulfill specific requirements, in particular being compatible with the other constituents of the mixture of enzymes and/or with endogenous active substances. In the present instance, there does not appear to be any suggestion or motivation provided for a person of skill in the art to try to modify Sipos to provide for the claimed enzymes and then to try to combine it with the teachings of Ogawa et al. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

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Reply dated March 10, 2005
Response to Office Action dated December 10, 2004

CONCLUSION

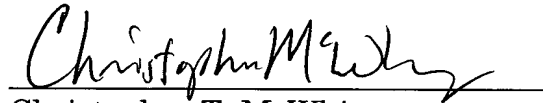
In view of the foregoing, the application is respectfully submitted to be in condition for allowance, and prompt favorable action thereon is earnestly solicited.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #029300.52497US).

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